REMARKS

In the present amendment, claims 1, 3, 8, 9, 10, 14, and 15 have been amended, claims 2, 4-7, and 11-13 have been cancelled, and new claim 16 has been added. Accordingly, claims 1, 3, 8-10 and 14-16 are pending in the application with claim 1 being independent. Of the pending claims, claims 1, 3, 8-10 and 16 are under consideration, and claims 14 and 15 are withdrawn from consideration.

Applicants note that the specification has been amended to remove the term "chicken" from the group of mammals listed on page 9 of the specification.

The claims have been amended to recite a transgenic mouse instead of a transgenic non-human mammal and to better comply with idiomatic English and standard U.S. practice.

New claim 16 has been added to more clearly express the decrease in the number of dopamine-producing neurons in the substantia nigra as compared to a wild type mouse. Support for new claim 16 can be found, for example, in Example 14 and Figure 11B of the present specification. Example 14 describes the quantification of dopamine producing neurons in the substantia nigra, and the results of the measurements are shown in Figure 11B. It can be seen in Figure 11B that the wild type mouse (Wild SNC – top section of left column) has about twice as many dopamine-producing neurons in comparison to the transgenic mouse (Tg SNC – top section of right column). The exact number for the dopamine-producing neurons shown in Figure 11B are 1,041 for the wild type mouse and 480 for the transgenic mouse. Based at least on these data, the recitation in new claim 16 of "at least 50% decrease in the number of dopamine-producing neurons" is supported.

No new matter has been added.

Information Disclosure Statement

Applicants note that the Examiner lined through most of the documents listed on a Form PTO-1449. Apparently, the Examiner had lined through the documents because they were duplicates, because they were in improper form for failing to identify the first author, or because copies were not provided.

Submitted concurrently herewith is a Supplemental IDS correcting the alleged deficiencies. A copy of only one document, Kim et al., is provided with the present Supplemental IDS, as this is the only document not previously provided by Applicants.

Response to Restriction Requirement

The Office Action maintains the restriction requirement and makes the requirement final. In response, Applicants respectfully request reconsideration of the requirement and rejoinder of the non-elected claims upon allowance of the elected claims.

Response to Rejections under 35 U.S.C. § 112, first paragraph

The Office Action rejects claims 1-13 under 35 U.S.C. § 112, first paragraph, as allegedly not enabled by the specification. The rejection states that the specification "while being enabling for a transgenic mouse whose genome comprises a nucleic acid sequence encoding mutant human α-synuclein operably linked to a tyrosine hydroxylase promoter . . . does not reasonably provide enablement for making any transgenic non-human mammal having decrease dopamine-producing neurons in the substantia nigra." Furthermore, the rejection asserts that the specification does not provide enablement "for making a transgenic mouse having decreased dopamine-producing neurons in the substantia nigra using a nucleic acid sequence encoding any α-synuclein or any promoter, or using any 'portion thereof' of a transgenic non-human mammal."

Applicants respectfully traverse the rejection. However, without expressing agreement with or acquiescence to the rejection, Applicants note that claims 1, 3, 8, 9, and 10 have been amended and claims 2, 4-7, and 11-13 have been cancelled. Applicants note that the present claims recite a transgenic mouse and do not include portions of a transgenic non-human mammal. Moreover, claim 1 has been amended to recite a human α-synuclein gene with a C-terminal deletion linked to a tyrosine hydroxylase promoter.

Applicants also respectfully provide the following comments pertaining to the enablement of the presently claimed invention. In the brain of a Parkinson's disease patient, which expresses the human α-synuclein gene without the A53T substitution, appearance of Lewy bodies where human α-synuclein is accumulated is observed. (Wakabayashi, K. et al., *Neurosci. Lett.* 239: 45 (1997),

attached hereto). Additionally, the human α-synuclein gene with a C-terminal deletion is more likely to be agglutinated *in vitro* as compared with the full-length human α-synuclein gene, regardless of the presence or absence of the A53T substitution (Serpell, L.C. et al., *PNAS USA* 97: 4897 (2000); see Figure 1 and page 4898, left column, "Results," attached hereto; Murray, I.V., et al., *Biochem.* 42: 8530 (2003); see Figure 1 and Abstract, attached hereto). The wild type human α-synuclein also is likely to be agglutinated *in vitro* by C-terminal deletion. That is, at least *in vitro*, C-terminal deletion rather than A53T substitution greatly contributes to the aggregability of the human α-synuclein.

In view of the state of the art at the time of filing of this application, the human α-synuclein gene with a C-terminal deletion, which is introduced into the mouse in the present invention, is not limited to the gene having A53T substitution. Even if any other human α-synuclein gene with a C-terminal deletion, which is likely to be agglutinated *in vitro* as mentioned above is introduced, the resultant transgenic mouse is likely to have a phenotype which is the same as or similar to the phenotype of the transgenic mouse of the Examples of the present application.

Further, it has been reported that the phenotype of the transgenic mouse wherein a human wild type α-synuclein gene with a deletion of the C-terminal 20 amino acids (without A53T substitution) is introduced is similar to the phenotype of the transgenic mouse of the present invention (Tofaris, G.K. et al., *J. Neurosci.* 36: 3942 (2006), attached hereto). This report supports the conclusion that the amino acid mutation in α-synuclein, such as the A53T substitution in human α-synuclein, is not essential for the expression of the phenotype of the transgenic mouse of the present invention.

In view of the foregoing comments and amendments, Applicants respectfully request withdrawal of the rejection.

Response to Rejections under 35 U.S.C. § 112, second paragraph

The Office Action rejects claims 1-13 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite.

Applicants respectfully traverse these rejections as well. As noted above, in an attempt to advance prosecution and without expressing agreement with or acquiescence to the rejection, claims 1, 3, 8, 9, and 10 have been amended and claims 2, 4-7, and 11-13 have been cancelled.

In view of the amendments of the claims and claim cancellations, Applicants respectfully request withdrawal of the indefiniteness rejections.

CONCLUSION

In view of the foregoing remarks and amendments, Applicants respectfully request withdrawal of the rejections of record and allowance of the pending claims.

Allowance of the application with an early mailing date of the Notice Allowance and Allowability is therefore respectfully requested. Should the Examiner have any further comments or questions, or wishes to discuss the matter, she is invited to call the undersigned at the telephone number indicated below.

Respectfully submitted,
Makoto YOSHIMOTO et al.

Sean Myers Payne

Bruce H. Bernstein
Reg. No. 29,027 42,920

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GREENBLUM & BERNSTEIN, P.L.C.
1950 Roland Clarke Place
Reston, VA 20191
(703) 716-1191